

=> s ondansetron  
L1 1411 ONDANSETRON

=> s l1 and hydrochloride monohydrate  
109789 HYDROCHLORIDE  
21116 MONOHYDRATE  
396 HYDROCHLORIDE MONOHYDRATE  
(HYDROCHLORIDE(W) MONOHYDRATE)  
L2 2 L1 AND HYDROCHLORIDE MONOHYDRATE

=> s ondansetron and methanolate  
1411 ONDANSETRON  
371 METHANOLATE  
L3 0 ONDANSETRON AND METHANOLATE

=> d l2 1-2 ibib abs hitstr

L2 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2002:353422 CAPLUS  
DOCUMENT NUMBER: 136:374797  
TITLE: Preparation of crystal and solvate forms of  
**ondansetron** hydrochloride for use as  
antiemetics  
INVENTOR(S): Lidor-Hadas, Ramy; Aronhime, Judith; Lifshitz,  
Revital; Weizel, Shlomit; Niddam, Valerie  
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva  
Pharmaceuticals USA, Inc.  
SOURCE: PCT Int. Appl., 46 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002036558	A2	20020510	WO 2001-US48720	20011030
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2002030935	A5	20020515	AU 2002-30935	20011030
US 2002107275	A1	20020808	US 2001-16752	20011030
PRIORITY APPLN. INFO.:			US 2000-244283P	P 20001030
			US 2000-253819P	P 20001129
			US 2001-265539P	P 20010131
			WO 2001-US48720	W 20011030

AB The present invention provides novel **ondansetron** hydrochloride cryst. polymorphic forms and solvates. Processes for making and interconverting the polymorphic forms are also provided. Further, pharmaceutical compns. contg. the novel polymorphic forms and hydrates for treating nausea and/or vomiting are described. For example, **ondansetron** base (400 mg) was suspended in 16 mL of a 1:1 mixt. of ethanol and isopropanol at room temp. and the suspension was heated to reflux to dissolve the **ondansetron**. After 20 min of stirring at reflux, an ethanolic soln. contg. 1.1 equiv of HCl was added. The reaction mixt. was stirred at this temp. for an addnl. 10 min. Evapn. of the solvent gave **ondansetron** hydrochloride dihydrate Form A.

L2 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2002:89819 CAPLUS  
DOCUMENT NUMBER: 136:139852  
TITLE: Drugs containing cilansetron for treating

non-obstipated male patients with irritable bowel syndrome  
INVENTOR(S): Cautreels, Werner; Steinborn, Claus Rudolf; Krause, Heinz Guenter; Caras, Steven David; Biesheuvel, Egbertus Hendrikus Evert; Plekkenpol, Albertus Hermannus Dirk  
PATENT ASSIGNEE(S): Solvay Pharmaceuticals G.m.b.H., Germany  
SOURCE: PCT Int. Appl., 10 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002007713	A2	20020131	WO 2001-EP8260	20010718
WO 2002007713	A3	20021114		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10123447	A1	20020207	DE 2001-10123447	20010514
US 2002040033	A1	20020404	US 2001-908735	20010720
PRIORITY APPLN. INFO.:			DE 2000-10036645 A	20000726
			DE 2001-10123447 A	20010514
			US 2000-220848P P	20000726

AB The invention relates to the use of cilansetron preps. for treating non-obstipated male patients with irritable bowel syndrome (IBS). Cilansetron is a 5HT3-receptor antagonist; other 5HT3-receptor antagonists can also be used to treat both genders. Thus tablets were prepd. that contained (parts): cilansetron **hydrochloride monohydrate** 4; corn starch 30; lactose 70; Kollidon-25 5; magnesium stearate 2; talc 3.

=> d his

(FILE 'HOME' ENTERED AT 10:34:46 ON 17 DEC 2002)

FILE 'CAPLUS' ENTERED AT 10:34:53 ON 17 DEC 2002

L1 1411 S ONDANSETRON  
L2 2 S L1 AND HYDROCHLORIDE MONOHYDRATE  
L3 0 S ONDANSETRON AND METHANOLATE

=> d l1 1409-1411 ibib abs hitstr

L1 ANSWER 1409 OF 1411 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:69896 CAPLUS

DOCUMENT NUMBER: 112:69896

TITLE: The effects of **ondansetron** (GR38032F) in

AUTHOR(S): rats and mice treated subchronically with diazepam  
Costall, Brenda; Jones, Brian J.; Kelly, M. Elizabeth;  
Naylor, Robert J.; Oakley, Nigel R.; Onaivi, Emmanuel  
S.; Tyers, Michael B.

CORPORATE SOURCE: Sch. Pharm., Univ. Bradford, Bradford, BD7 1DP, UK  
SOURCE: Pharmacology, Biochemistry and Behavior (1989), 34(4),  
769-78  
CODEN: PBBHAU; ISSN: 0091-3057

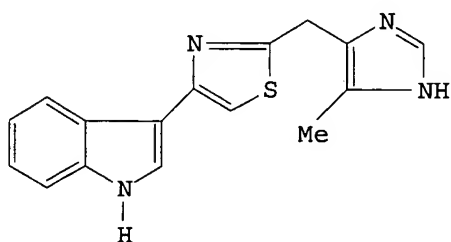
DOCUMENT TYPE: Journal

LANGUAGE: English

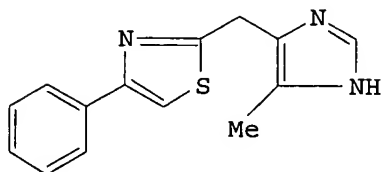
AB Using rat and mouse models of aversive behavior, the properties of the 5-HT3 receptor antagonist **ondansetron** (GR38032F) that are relevant to its proposed use as an anxiolytic agent were investigated.

Tolerance to the disinhibitory properties of diazepam was readily demonstrated in the social interaction test in the rat, but did not occur after subchronic treatment with **ondansetron**. In both the light/dark exploration test in mice and the social interaction test in rats, withdrawal from subchronic treatment with diazepam increased behavior suppression, whereas this was not obsd. with **ondansetron**. The behavioral suppression and wt. loss induced by either the withdrawal of diazepam or the administration of the benzodiazepine receptor antagonist, flumazenil, in animals treated subchronically with diazepam, was prevented or antagonized by diazepam or **ondansetron**. Buspirone was ineffective. It is concluded that, in rats and mice, tolerance to the disinhibitory effects of **ondansetron** does not occur, that withdrawal from subchronic treatment with **ondansetron** is not assocd. with any behavioral disturbances and that **ondansetron** is highly effective in preventing the behavioral suppression and wt. loss following withdrawal from subchronic diazepam treatment. These data suggest that **ondansetron** may have major therapeutic advantages over currently available anxiolytic agents, particularly in patients who have previously received prolonged benzodiazepine therapy.

L1 ANSWER 1410 OF 1411 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1990:55689 CAPLUS  
 DOCUMENT NUMBER: 112:55689  
 TITLE: Aromatic thiazole derivatives: structurally novel and selective serotonin-3 receptor antagonists  
 AUTHOR(S): Nagel, Arthur A.; Rosen, Terry; Rizzi, James; Daffeh, June; Guarino, Karen; Nowakowski, Jolanta; Vincent, Lawrence A.; Heym, James; McLean, Stafford; et al.  
 CORPORATE SOURCE: Dep. Med. Chem., Pfizer Cent. Res., Groton, CT, 06340, USA  
 SOURCE: Journal of Medicinal Chemistry (1990), 33(1), 13-16  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 112:55689  
 GI



I



II

AB This report discloses the discovery of a novel series of potent serotonin-3 5-HT<sub>3</sub> antagonists, represented by prototypical structures I and II, in which a thiazole ring system appears to mimic the ester functionality in ICS-205-930 and the carbonyl moiety in **ondansetron**. Furthermore, removal of the 5(4)-Me group from the imidazole functionality in compds. I and II causes the resulting compds. to display an initial bradycardia response in the von Bezold-Jarisch reflex, similar to the known 5-HT<sub>3</sub> agonist 2-methylserotonin.

LINE ANSWER 1411 OF 1411 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1990:49238 CAPLUS  
DOCUMENT NUMBER: 112:49238  
TITLE: 5-HT3 receptors mediate inhibition of acetylcholine  
release in cortical tissue  
AUTHOR(S): McLean, Stafford; Rosen, Terry  
CORPORATE SOURCE: Pfizer Cent. Res., Groton, CT, USA  
SOURCE: Chemtracts: Organic Chemistry (1989), 2(5), 325-7  
CODEN: CMOCEI; ISSN: 0895-4445  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Based on the results of a series of in vitro studies, it was shown that activation of 5-HT3 receptors can reduce the evoked release of acetylcholine from the cerebral cortex. Furthermore, it was demonstrated that the selective 5-HT3 antagonists **ondansetron** and **zacopride** block the inhibitory effect of 2-methylserotonin (5-HT3 agonist) on K-stimulated [3H]acetylcholine release.